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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,853	11/07/2000	Fulvio Mavilio	1303-110	5693

7590

09/26/2002

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 09/26/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/674,853

Applicant(s)

MAVILIO, FULVIO

Examiner

Anne M Wehbé

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 July 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's amendment and response received on 7/1/02 has been entered. Claims 1-10 are pending in the instant application. Applicant's amendment of the specification to include an abstract on a separate page is acknowledged. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in previous office actions.

Priority

Applicant's submission of a copy of the PTO/DO/EO/903 which indicates that the priority document was received by the Office perfects applicant's claim of priority to the application filed in Italy on 5/08/98.

Specification

The objection to the specification is withdrawn in view of applicant's submission of an abstract of the instant invention on a separate piece of paper.

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Claim Rejections - 35 USC § 112

The rejections of claims 2, 4, and 5 under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's amendment to these claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Watt et al. in view of Choi et al. and Murry et al. is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the methods taught by Watt et al. result in the spontaneous conversion of the transfected dermal fibroblasts to muscle cells in vivo, and that the rate of spontaneous conversion is too low to make this methodology practical for treating muscle disorders in a patient. In contrast, the applicant states that their methods result in a higher frequency of myogenic conversion than that observed by Watt et al. In response, please note that the applicant claims do not recite the treatment of muscle disorders, nor do they recite methods of increasing the frequency of myogenic conversion. The claims of record are simply methods of preparing genetically modified fibroblasts which express a muscle lineage commitment gene and a therapeutic gene, and genetically-modified fibroblasts made using this method. The rate at which

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the fibroblasts convert to muscle cells is not relevant to the applicant's claims as written. As such, applicant's arguments regarding alleged differences in rates of myogenic conversion between their methods and the methods taught by Watt et al. are not on point. The essential teachings of Watt et al. cited in the previous office action are the transduction of dermal fibroblasts which have been removed from a patient with a muscular disorder with a vector encoding dystrophin, a gene therapeutic for muscular dystrophy. The applicant has not refuted that Watt et al. does in fact teach this method of genetically modifying fibroblasts.

The applicant further argues that Choi et al. does not supplement Watt et al. because Choi et al. teaches the use of an integrating retroviral vector and that the rate of myogenic conversion using this vector is low. Again, this line of reasoning does not relate to applicant's claims as written. The claims do not place limitations on the rate of myogenic conversion or even mention myogenic conversion as a result of the genetic modification of the fibroblasts. Furthermore, please note that only claims 4-5 place any limitation on the type of vector or virus used. The remaining claims broadly read on the use of any type of vector or viral vector whether integrating or non-integrating. Choi et al. was cited in the previous office action for providing the teaching that fibroblasts which express myoD convert to myoblasts.

Applicant's concern that Murry et al. does not teach the frequency of myogenic conversion of the cardiac fibroblasts is not apposite to the applicant's actual claims. In particular, please note that the claims broadly recite fibroblasts and are not limited to any particular kind of

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fibroblast such as a dermal fibroblast. Murry et al. is cited in the previous office action for teaching the infection of fibroblasts with an adenovirus encoding myoD.

Furthermore, the combined teachings of Watt et al. , Choi et al. and Murry et al. were cited for providing motivation for combining the expression of dystrophin and myoD in fibroblasts. Motivation for making a fibroblast with this combination of genes is found in the teachings of Watt et al. that one would not wish to transduce/transfect primary myoblasts with dystrophin from patients with muscle disease and in the teachings of Murry and Choi that fibroblasts transduced with myoD are capable of converting to muscle cells. Based on these teachings the skilled artisan would be motivated to transduce the primary fibroblasts expressing dystrophin taught by Watt et al. with either of the vectors encoding myoD taught by Murry and Choi in order to produce myoblasts in vitro which express dystrophin. The rate of myoconversion or the number of myoblasts produced is irrelevant to the motivation to simply make fibroblasts which have been genetically modified to comprise the dystrophin gene and the myoD gene.

The applicant is also reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In summary, applicant's argument are based on the premise that the references fail to show certain features of applicant's invention; however, as discussed in detail above, the features upon which applicant relies (i.e., rate of myogenic conversion, type of fibroblasts, types of muscle cells, and types of vectors) are not recited in the rejected claims.

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Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries

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should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in cursive script, appearing to read 'Anne M. Wehbé', written in black ink.